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Patentanmeldung Nr. | Patent application No. | Demande de brevet n°

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Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
p.o.

R C van Dijk

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Boehringer Ingelheim International GmbH
Binger Strasse 173
55216 Ingelheim am Rhein
ALLEMAGNE

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Combinations of epinastine and vitamins B group as new pharmaceutical formulations for treatment of skin disease

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Combinations of Epinastine and vitamins B group as new pharmaceutical formulations for treatment of skin disease

The present invention relates to new pharmaceutical formulations in the treatment of skin diseases comprising an antihistaminic-effective amount of Epinastine or a pharmaceutically acceptable salt thereof as a pharmacologically active compound, and at least on vitamin of the B group. The formulations described in the present invention also include pharmaceutically acceptable carriers and excipients.

Moreover, this invention relates to the use of these formulations to treat pruritus (itching) derived from skin disease such as urticaria, eczema, and skin irritation.

Remarkably, the formulations described in the present invention are highly effective for treatment of skin diseases associated with allergic reactions.

Background of the invention

In recent years, changes in diet and life style, air pollution, increased exposure to environmental chemicals due to various factors of deterioration in environmental conditions or increased stress from the social life have been contributing to an increased incidence of developing skin diseases associated with allergic reactions such as urticaria, eczema, skin irritation, and dermatitis. Skin diseases accompanying itching represented by pruritus, psoriasis vulgaris are also prevailing in number.

It is emphasized that improvements in surroundings such as elimination of causative antigens are the most important factor for the treatment of these skin diseases, particularly for allergic skin disease. Nevertheless, as already reviewed, pathogenic causes are often fallible to be identified since they are varied and complicated. For the above reasons, formulations combining antihistaminic compounds are helpful in the treatment of these symptoms.

At the same time, liquid-type formulations for cold and rhinitis combined with

loxoprofen sodium, dihydrocodeine phosphate, Epinastine hydrochloride, dl-methylephedrine hydrochloride, ambroxol hydrochloride, anhydrous caffeine, vitamin B_1 nitrate, and vitamin B_2 as pharmacological active compounds are disclosed in Example 4 of Publication of Japanese Patent Application JP2001-199882A.

Liquid-type formulations for cold combined with loxoprofen sodium, dihydrocodeine phosphate, Epinastine hydrochloride, dl- methylephedrine hydrochloride, ambroxol hydrochloride, anhydrous caffeine, vitamin B_1 nitrate, and vitamin B_2 as pharmacological active compounds are disclosed in Example 4 of Publication of Japanese Patent Application JP2001-172175A.

Tablet-type antitussive agent for cold combined with ibuprofen, Epinastine hydrochloride, noscapine, benproperine phosphate, ambroxol hydrochloride, trimetoquinol hydrochloride, anhydrous caffeine, vitamin B_1 nitrate, and vitamin B_2 as pharmacological active compounds is disclosed in Example 4 of Publication of Japanese Patent Application JP10-017473A.

These examples are combination medicines of epinastine, vitamin B_1, vitamin B_2, etc. All these medicines are cold remedies.

The use of a combination of Epinastine and a vitamin of the b group in the treatment of skin diseases in association with allergic reactions is new.

Objective of the present invention

The present invention aims to provide compositions for the treatment of skin diseases that exert its significant utility to achieve effective improvements.
In addition, the present invention intends to provide the compositions for treatment of skin diseases by employing highly effective pharmaceutical compounds for significant improvements on symptoms of skin diseases accompanying itching, particularly urticaria, eczema, skin fit, dermatitis, pruritus, eruption, and psoriasis vulgaris accompanying itchy sensation.

Description of the Invention

The present invention relates to the pharmaceutical formulations for the treatment of skin disease comprising an antihistaminic-effective amount of Epinastine or its pharmaceutically acceptable salt thereof as pharmacologically active compound, and vitamin B group.

Epinastine, (±) 3-amino-9, 13b-dihydro-1H-dibenz [c, f] imidazo [1,5-a] azepine, the hydrochloride thereof respectively, is a drug possessing H1-antihistaninic property. It primarily has been used to treat allergic reaction of the eyes and the nasal mucosa.

In the composition of the present invention Epinastine preferably is taken in the form of a salt such as the hydrochloride, hydrobromide, oxalate, nitrate, sulfonate, fumarate, maleate, sulfate, and phosphate. The free base can be taken, too. Preferred is Epinastine-hydrochloride.

The amount of Epinastine or a pharmacologically acceptable salt thereof depends on the application route.

In the case of oral application, the daily dosage in equivalent quantity of Epinastine-hydrochloride for an adult is between 2 and 20mg, preferably between 5 and 15 mg, and further more preferably between 7.5 and 12.5 mg. Preferably, this amount is given via one or more dosage units.

In the case of topical application the amount in equivalent quantity of Epinastine hydrochloride is between 1 and 50 mg per 1 g of composition, preferably between 2 and 30 mg per 1 g of composition, and further more preferably between 5 and 15 mg per 1 g of composition.

According to the invention there is provided a pharmaceutical formulation for the treatment of skin diseases including at least on vitamin of the B group in addition to Epinastine. B group vitamins are regarded as a vitamin group having important influences on metabolism of protein, lipid, and carbohydrate by becoming components of coenzyme in the human vivo, or by being coenzyme itself, and help

normalize the organism such as skin, nail, hair, and mucosa.

B group vitamins used in the pharmaceutical formulations for treatment of skin disease described in the present invention include vitamin-like active substances such as vitamin B_1 such as thiamine, thiamine hydrochloride, thiamine nitrate, thiamine disulfide nitrate, thiamine disulfide, thiamine dicetylsulfate salt, dicethiamine hydrochloride, fursultiamine hydrochloride, fursultiamine, octotiamine, cycotiamine, bisibutiamine, bisbentiamine, prosultiamine, benfotiamine, cocarboxylase and dibenzoylthiamaine, and its salt and derivatives thereof, vitamin B_2 such as riboflavin, riboflavin butyrate, riboflavin sodium phosphate and flavin adenine dinucleotide, and its salt and derivatives thereof, vitamin B_6 such as pyridoxine, pyridoxal, pyridoxamine, pyridoxine phosphate, pyridoxal phosphate and pyridoxamine phosphate, and its salt and derivatives thereof, vitamin B_{12} such as cobalamin, cyanocobalamin, hydroxocobalamin, hydroxocobalamin acetate and mecobalamin, and its salt and derivatives thereof, niacin such as nicotinic acid, nicotinamide, inositol hexanicotinate and hepronicate, and its salt and derivatives thereof, pantothenic acid such as calcium pantothenate, sodium pantothenate, panthenol and pantethine, and its salt and derivatives thereof, biotin, vitamins such as folic acid, orotic acid such as orotic acid and choline orotate, and its salt and derivatives thereof, thioctic acid such as thioctic acid (lipoic acid) and thioctic acid amide, and its salt and derivatives thereof, p-aminobenzoic acid and its salt and derivatives thereof, inositol such as inositol and inositol hexanicotinate, and its salt and derivatives thereof, carnitine such as carnitine, carnitine chloride and acetyl-carnitine and its salt and derivatives thereof, and choline such as choline and choline orotate and its salt and derivatives thereof.

One or more compounds of these B group vitamins can be used to formulate this invention.

Preferred are the following combinations of Epinastine plus one vitamin of the vitamin B group:
Epinastine plus
vitamin B_1,

vitamin B_2,
vitamin B_6,
vitaminB_{12},
niacin,
pantothenic acid,
biotin,
folic acid,
orotic acid,
thioctic acid,
p-aminobenzoic acid,
inositol,
carnitine,
choline, or a salt or derivatives of each.

If the combination shall comprise at least two vitamins of the vitamin B group, the two vitamins preferably are:
- riboflavin or riboflavin butyrate and pyridoxine hydrochloride,
- thiamin nitrate and riboflavin or riboflavin butyrate,
- pyridoxine hydrochloride and thiamin nitrate,
- nicotinamide and pyridoxine hydrochloride,
- nicotinamide and thiamin nitrate,
- nicotinamide and riboflavin or riboflavin butyrate,
- pyridoxine hydrochloride and tocopherol acetate.

If the combination shall comprise at least three vitamins of the vitamin B group, the three vitamins preferably are:
- thiamin nitrate, riboflavin or riboflavin butyrate, pyridoxine hydrochloride,
- thiamin nitrate, riboflavin or riboflavin butyrate, nicotinamide,
- thiamin nitrate, nicotinamide, pyridoxine hydrochloride,
- nicotinamide, riboflavin or riboflavin butyrate, pyridoxine hydrochloride,
- pyridoxine hydrochloride, riboflavin sodium phosphate, panthenol.

If the combination shall comprise at least four vitamins of the vitamin B group, the

four vitamins preferably are:
thiamin nitrate, riboflavin butyrate, pyridoxine hydrochloride, nicotinamide.

Of any of the named vitamins another salt form may be used instead of the named one.

Furthermore, other pharmaceutical active substances may be combined to formulate this invention in addition to Epinastine and B group vitamins. Examples comprise of sulfur-containing amino acid such as cysteine, methionine, aminoethylsulfonic acid and glutathione, antioxidant vitamins such as vitamin C, vitamin E and vitamin A, antioxidant vitamin-like substances such as ubiquinone, pangamic acid and flavonoid, D group vitamins such as ergocalciferol and cholecalciferol.

Although combination amount of B group vitamins to formulate the present invention varies depending on types of B group vitamins, for oral use given daily to an adult lies in the range from 0.0001 to 1500 mg, and for topical use it lies in the range from 0.1 to 200 mg/g.

In further details, combination amount of vitamin B_1 and its salt and derivatives thereof for oral use given daily to an adult lies normally in the range from 0.1 to 500 mg, preferably in the range from 0.5 to 200 mg, and more preferably in the range from 1 to 100 mg, and for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of vitamin B_2 and its salt and derivatives thereof for oral use given daily to an adult lies normally in the range from 0.5 to 180 mg, preferably in the range from 1 to 90 mg, and more preferably in the range from 2 to 45 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of vitamin B_6 and its salt and derivatives thereof for oral use

given daily to an adult lies normally in the range from 0.1 to 500 mg, preferably in the range from 1 to 200 mg, and more preferably in the range from 5 to 100 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of vitamin B_{12} and its salt and derivatives thereof for oral use given daily to an adult lies normally in the range from 0.0001 to 15 mg, preferably in the range from 0.0005 to 3 mg, and more preferably in the range from 0.001 to 1.5 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of niacin and its salt and derivatives thereof for oral use given daily to an adult lies normally in the range from 0.1 to 1000 mg, preferably in the range from 1 to 800 mg, and more preferably in the range from 12 to 400 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of pantothenic acid and its salt and derivatives thereof for oral use given daily to an adult lies normally in the range from 0.1 to 120 mg, preferably in the range from 1 to 60 mg, and more preferably in the range from 5 to 30 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of biotin for oral use given daily to an adult lies normally in the range from 0.001 to 10 mg, preferably in the range from 0.005 to 1 mg, and more preferably in the range from 0.01 to 0.5 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of folic acid for oral use given daily to an adult lies normally in the range from 0.01 to 100 mg, preferably in the range from 0.05 to 20 mg, and more preferably in the range from 0.1 to 10 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more

preferably in the range from 1 to 15 mg/g.

Combination amount of orotic acid and its salt and derivatives thereof for oral use given daily to an adult lies normally in the range from 1 to 500 mg, preferably in the range from 5 to 200 mg, and more preferably in the range from 10 to 100 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of thioctic acid and its salt and derivatives thereof for oral use given daily to an adult lies normally in the range from 0.1 to 500 mg, preferably in the range from 1 to 200 mg, and more preferably in the range from 2 to 100 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of p-aminobenzoic acid and its salt and derivatives thereof for oral use given daily to an adult lies normally in the range from 1 to 1500 mg, preferably in the range from 2 to 1000 mg, and more preferably in the range from 10 to 500 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of inositol and its salt and derivatives thereof for oral use given daily to an adult lies normally in the range from 1 to 800 mg, preferably in the range from 5 to 400 mg, and more preferably in the range from 10 to 200 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of carnitine and its salt and derivatives thereof for oral use given daily to an adult lies normally in the range from 1 to 1000 mg, preferably in the range from 2 to 600 mg, and more preferably in the range from 10 to 100 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

Combination amount of choline and its salt and derivatives thereof for oral use given daily to an adult lies normally in the range from 1 to 1500 mg, preferably in the range from 2 to 1000 mg, and more preferably in the range from 10 to 500 mg. And for topical use it lies normally in the range within 200 mg/g, preferably in the range from 0.1 to 50 mg/g, and more preferably in the range from 1 to 15 mg/g.

It is possible that the pharmaceutical formulations described in the present invention are orally given all at once or in divided doses. For topical purposes the daily amount can be applied all at once or it can be divided in doses. The topical application should occur directly onto the affected region of skin. Dose adjustment of Epinastine and B group vitamins may reflect age, body weight, and manifesting symptoms.

In addition, when the pharmaceutical formulations described in the present invention are orally given, part of or all of B group vitamins, may be formulated in a slow release form while Epinastine itself or a combination of Epinastine and B group vitamins are formulated for instant release. When other additional active components are present, they may be in either of the two formulation parts, the instant or the slow release part of the formulation in accordance with the pharmacokinetic characteristic of each active component.

The two essential components of the present invention epinastine and the at least one vitamin of the B group can be combined together in one pharmaceutical preparation or the two combinations are formulated separately from each other in two pharmaceutical preparations and then given together or in close timely proximity, i.e. within 12 hours, preferably within 1 hour more preferably within 15 minutes and in particular preferred within 2 minutes.
Preferred are pharmaceutical compositions that contain both ingredients, i.e. the both ingredients are not separated.

These fast release components and slow release components may be present in one application unit each. The two components may be formulated separately and then they are combined physically in one dosage unit, f. e. a capsule or the like or they are

applied together. In an alternative embodiment the fast release components and slow release components may be regarded as one unit formulation. Such unit formulations may include for example multilayer tablets combining fast release layer(s) and slow release layer(s), granules combining fast release granules and slow release granules or capsules filled with the granules, hard capsules filled with a combination of small fast release tablet(s) and slow release tablet(s), and dry syrup or suspension syrup using microcapsule or microsphere as slow release components.

The pharmaceutical compositions described in the present invention can be used in any oral form such as tablets, granules, fine granules, powders, capsules, caplets, soft capsules, pills, suspensions, emulsions, oral solutions, syrups, dry syrups, chewable forms, forming tablets, drops, and orally disintegrable tablets, and in any topical form such as creams, ointments, gel ointments, suppositories, poultices, tapes, topical solutions, aerosols, lotions, and foams. In addition, preparation formed into microparticles such as microcapsule, nanocapsules, microspheres, nanospheres, liposomes may be also included in the aforementioned compositions.

Moreover, the properties of the inventive composition such as stability, release, continuance, disintegration, distinglation, dissolution, concealment of taste, improvement in usage etc. can be regulated by the addition of additives known in the art.

For example, the pharmaceutically active substance can be dispensed in separate granules, multi-layer granules, multi-layer tablets or dry coated tablets, tablets of separated granules, microcapsules, etc. Coating preparations such as sugarcoated tablets, film coating tablets, coating granule, foaming pharmaceutical preparation can be used as well as chewable preparations, in the mouth dissolving preparations, matrix preparations, together with comminutions, solid solutions, etc. Sweetening agents, refrigerants, antioxidants or stabilizing agents, agents adjusting a certain pH-value can be added as well as the viscosity, the osmotic pressure or the salt concentration influencing agents. These methods can also be combined.

Optionally, also the following additives can be added: excipients, bases, binders, disintegrators, lubricants, superplasticizers, coating agents, sugar coating agents, plasticizers, antifoaming agents, polish, foaming agents, antistatic agents, desiccant, moisturizing agents, surfactant, solubilizer, buffer agents, resolvents, solubilizing agents, solvents, diluents, stabilizers, emulsifying agents, suspension, suspending agents, dispersing agents, isotonizing agents, aerosol propellant, adsorbents, reducing agents, antioxidant, backing, wetting agents, wet modifier, filler, extender, adhesives, viscous agent, softeners, pH modifiers, antiseptics, preservatives, sweetening agents or preferably bitter taste masking agents like sodium dodecylsulfate (sodium lauryl sulfate), corrigent, refrigerative agents, flavoring agents, perfume, fragrance, coloring matters, and the like. Any of these additives may be used in the regular compositions methods, and do not impose any limitation to such composition methods.

Examples of these additives are explained in the Japanese Pharmaceutical Excipients Directory 2000 (Japan Pharmaceutical Excipients Council edit, Yakuji Nippo. Ltd. issue).

These preparations can be manufactured in the usual manner, f.e. by adding preparation additives to the pharmacologically active substance.

The compositions described in the present invention are explained by examples which follow. However, the present invention of the pharmaceutical compositions is not limited to these examples.

Examples

Any of the examples may comprise a sweetener or preferably a bitter taste masking agent, like for example sodium dodecylsulfate (sodium lauryl sulfate) in an amount of less than 300 mg for a daily dosage.

Example 1

Powder

The following ingredients were homogeneously mixed. The resulted mixed particles

were divided into portions of 800 mg to prepare powder compositions.

Epinastine hydrochloride	20.0 g
Riboflavin	24.0 g
Pyridoxine hydrochloride	100.0 g
Calcium pantothenate	60.0 g
L-cysteine	320.0 g
Biotin	0.1 g
Orotic acid	400.0 g
Thioctic acid amide	20.0 g
p-Aminobenzoic acid	600.0 g
Corn starch	1167.9 g
Lactose	2040.0 g
Magnesium stearate	48.0 g

Example 2

Tablet

The following ingredients were homogeneously mixed. The resulted mixed particles were compressed with a mold to prepare tablets at 150 mg each.

Epinastine hydrochloride	30 g
Thiamin nitrate	45 g
Riboflavin butyrate	36 g
Pyridoxine hydrochloride	135 g
Nicotinamide	450 g
Calcium pantothenate	90 g
Lactose	933 g
Microcrystalline cellulose	945 g
Light anhydrous silicic acid	18 g
Talc	9 g
Magnesium stearate	9 g

Example 3

Tablet

The following ingredients were homogeneously mixed. The resulted mixed particles were compressed with a mold to prepare tablets at 250 mg each.

Epinastine hydrochloride	20 g
Pyridoxal phosphate	24 g
Riboflavin butyrate	24 g
Inositol	36 g
Aminoethyl sulfonic acid	72 g
Panthenol	120 g
Carnitine chloride	100 g
Biotin	1 g
Folic acid	20 g
Lactose	513 g
Microcrystalline cellulose	546 g
Light anhydrous silicic acid	12 g
Talc	6 g
Magnesium stearate	6 g

Example 4

Oral solution

The following ingredients were dissolved in sterile purified water, added with sodium hydrate to adjust at pH 5, and diluted with sterile purified water to get a total volume of 20 L. The resulted solution was transferred in portions of 50 mL into glass bottles to provide oral solutions.

Epinastine hydrochloride	4 g
Aminoethylsulfonic acid	80 g
Inositol	20 g
Thiamin nitrate	4 g
Riboflavin sodium phosphate	4 g
Pyridoxine hydrochloride	4 g
Carnitine chloride	40 g

Nicotinamide	10 g
Calcium pantothenate	8 g
Orotic acid choline	40 g
Cyanocobalamin	0.004 g
Thioctic acid	2 g
Citric acid	50 g
Sodium citrate	10 g
Purified sucrose	2400 g
Caramel*	60 g
Sodium hydrate	Adequate amount
Antiseptics	Adequate amount
Flavor	Trace amount
Sterile purified water	Adequate amount

* instead of Caramel sodium dodecylsulfate in an amount of up to 300 mg per day may be used.

Example 5

Syrup

The following ingredients were dissolved in sterile purified water, added with citric acid to adjust at pH 2.5, and then diluted with sterile purified water to prepare syrup at the total volume of 10 L.

Epinastine hydrochloride	20 g
Pyridoxine hydrochloride	20 g
Riboflavin sodium phosphate	40 g
Panthenol	60 g
Purified sucrose	4000 g
Sodium chloride	30 g
Sodium citrate	20 g
Citric acid	Adequate amount
Antiseptics	Adequate amount

Flavor	Trace amount
Sterile purified water	Adequate amount

Example 6

Sugarcoated tablet

The following ingredients were processed through a regular method to provide mixed particles, and the particle was compressed to form tablets at 250 mg each.

Epinastine hydrochloride	10 g
Calcium pantothenate	15 g
Ascorbic acid	200 g
L-cysteine	160 g
Corn starch	603 g
Lactose	740 g
Microcrystalline cellulose	360 g
Hydroxypropylcellulose	90 g
Light anhydrous silicic acid	45 g
Talc	18 g
Magnesium stearate	9 g

Subsequently, the tablets were transferred into a coating pan, and coated using coating solution. The equal volume mixture of ethyl alcohol contained 5% weight/volume of hydroxypropylmethylcellulose and purified water to increase in weight/volume by 10 mg per one tablet. Next, 2% weight/volume of talc, 2% weight/volume of titanium oxide, 3% weight/volume of calcium carbonate, 1% weight/volume of powdered acacia, and aqueous solution containing 60% weight/volume of purified sucrose were used to coat tablets to give increase in weight/volume by 100 mg per one tablet. Finally, aqueous solution containing 60% weight/volume purified sucrose was used to coat tablets to give an increase in weight/volume by 100 mg per one tablet. Thus sugarcoated tablets were prepared.

Example 7

Granules

The following ingredients were prepared as granules through a regular method to prepare mixed particles, and packed to give an amount of 1000 mg per one pack for

granules.

Epinastine hydrochloride	10 g
Thiamin nitrate	5 g
Riboflavin	5 g
Pyridoxine hydrochloride	10 g
Nicotinamide	10 g
DL-methionine	1000 g
Calcium carboxymethylcellulose	240 g
Mannitol	1100 g
Corn starch	478 g
Tartaric acid	100 g
Aspartame*	20 g
Acesulfame potassium	20 g
Fragrant materials	2 g

*instead of aspartame sodium dodecylsulfate in an amount of up to 300 mg per day may be used.

Example 8

Cream

The following ingredients were processed through a regular method to form a cream of a total weight of 1kg, added with sodium citrate to adjust at pH 5.

Epinastine hydrochloride	10.0 g
Pyridoxine hydrochloride	1.0 g
Tocopherol acetate	10.0 g
Medium chain fatty acid triglyceride	200.0 g
Propylene glycol	150.0 g
Glyceryl monostearate	80.0 g
Polyoxyethylene cetyl ether	40.0 g
Diisopropyl adipate	50.0 g
Citric acid	0.1 g
Sodium citrate	Adequate amount

Antiseptics	Adequate amount
Purified water	Adequate amount

Claims

1. A pharmaceutical formulation for the treatment of skin disease, combining Epinastine or a pharmaceutically acceptable salt thereof as pharmacologically active compound, and at least on vitamin of the vitamin B group.

2. The pharmaceutical formation according to claim 1, characterized in that the formulation is for oral use.

3. The pharmaceutical formation according to claim 1, characterized in that the formulation is for oral use.

4. The pharmaceutical formation according to claim 1, characterized in that the amount of Epinastine or its pharmaceutically acceptable salt thereof for oral use daily given to an adult lies in the range from 2 to 20 mg in equivalent to quantity to Epinastine hydrochloride.

5. The pharmaceutical formulation according to claim 1, characterized in that the amount of Epinastine or a pharmaceutically acceptable salt thereof for topical use lies in the range from 1 to 50 mg in equivalent quantity to Epinastine chloride per 1 g of the formulations.

6. The pharmaceutical formulation according to claim 1, characterized in that the daily dose of the at least one vitamin of the B group vitamins lies in the range from 0.0001 to 1500 mg.

7. The pharmaceutical formulation according to claim 1, characterized in that the amount of the at least one vitamin of the B group vitamins for topical use lies in the range from 0.1 to 200 mg per 1 g of the formulation.

8. The pharmaceutical formulation according to claim 1, characterized in that the at least one vitamin of the B group vitamins is selected from vitamin B_1, vitamin B_2, vitamin B_6, vitaminB_{12}, niacin, pantothenic acid, biotin, folic acid, orotic acid,

thioctic acid, p-aminobenzoic acid, inositol, carnitine, and/or choline, and its salt and derivatives thereof.

9. The pharmaceutical formulation according to claim 1, characterized in that the formulation comprises one vitamin of the vitamin B group only.

10. The pharmaceutical formulation according to claim 1, characterized in that the formulation comprises two vitamins of the vitamin B group.

11. The pharmaceutical formulation according to claim 1, characterized in that the formulation comprises three vitamins of the vitamin B group.

12. Use of a pharmaceutical formulation according to any of claims 1 to 11 for the manufacture of a medicament for the treatment of a skin disease.

13. Use according to claim 12 for the manufacture of a medicament for the treatment of a skin disease associated with an allergic reaction.

14. Use according to any of claims 12 or 13 for the manufacture for a medicament for oral application.

15. Use according to any of claims 12 or 13 for the manufacture for a medicament for topical application.

16. Method for the treatment of a skin diseases, whereby a formulation according to any of claims to 11 is applied.

17. Method according to claim 16, whereby the method is for a skin disease associated with an allergic reaction.

18. Method according to any of claims 16 or 17, wherein the formulation is applied orally or topically.

Abstract

The present invention relates to new pharmaceutical compositions for the treatment of skin disease comprising an antihistaminic-effective amount of Epinastine or pharmaceutically acceptable salt thereof as pharmacologically active compound, and one or more B group vitamins. The formulations described in the present invention additionally include pharmaceutically acceptable carriers and excipients.